



Since January 2020 Elsevier has created a COVID-19 resource centre with free information in English and Mandarin on the novel coronavirus COVID-19. The COVID-19 resource centre is hosted on Elsevier Connect, the company's public news and information website.

Elsevier hereby grants permission to make all its COVID-19-related research that is available on the COVID-19 resource centre - including this research content - immediately available in PubMed Central and other publicly funded repositories, such as the WHO COVID database with rights for unrestricted research re-use and analyses in any form or by any means with acknowledgement of the original source. These permissions are granted for free by Elsevier for as long as the COVID-19 resource centre remains active.

Journal Pre-proof

Bee venom and SARS-CoV-2

Wei Yang, Fu-liang Hu, Xiao-feng Xu

PII: S0041-0101(20)30224-5

DOI: <https://doi.org/10.1016/j.toxicon.2020.04.105>

Reference: TOXCON 6339

To appear in: *Toxicon*

Received Date: 19 April 2020

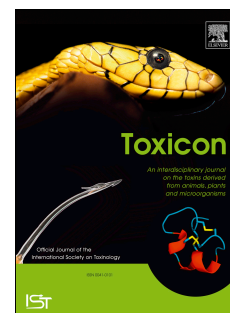
Revised Date: 27 April 2020

Accepted Date: 27 April 2020

Please cite this article as: Yang, W., Hu, F.-l., Xu, X.-f., Bee venom and SARS-CoV-2, *Toxicon* (2020), doi: <https://doi.org/10.1016/j.toxicon.2020.04.105>.

This is a PDF file of an article that has undergone enhancements after acceptance, such as the addition of a cover page and metadata, and formatting for readability, but it is not yet the definitive version of record. This version will undergo additional copyediting, typesetting and review before it is published in its final form, but we are providing this version to give early visibility of the article. Please note that, during the production process, errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

© 2020 Published by Elsevier Ltd.



Bee venom and SARS-CoV-2
Wei Yang^{1*}, Fu-liang Hu², Xiao-feng Xu¹

¹Oncology, Hangzhou Red Cross Hospital, 208 Huancheng East Road, Hangzhou 310003, Zhejiang, China.

²College of Animal Science, Zhejiang University, 886 YuHangTang Road, Hangzhou 310058, Zhejiang, China.

*Correspondence: Wei Yang, Tel: 13754326795; E-mail: maxwell1941@126.com

According to data from Johns Hopkins Coronavirus Resource Center, the global number of confirmed COVID-19 case exceeded 2.0 million on the 15th of April. I am a physician, and I participated the prevention and control of coronavirus in China.

There is one discovery we would like to report here. It reminds us the story of the discovery of cowpox and the eventual victory of humans over this disease (Bennet and Baxby, 1996). In Hubei province, the epicentre of COVID-19 in China, the local beekeepers association conducted a survey of beekeepers (Fig. 1). A total of 5,115 beekeepers were surveyed from February 23 to March 8, including 723 in Wuhan, the outbreak epicentre of Hubei. None of these beekeepers developed symptoms associated with COVID-19, and their health was totally normal. After that, we interviewed five apitherapists in Wuhan and followed 121 patients of their apitherapy clinic. These patients had received apitherapy from October 2019 to December 2019, and all the five bee apitherapists have the habit of self-apitherapy for their own health care (apitherapy means making use of bee venom from the honeybee's sting to treat or prevent certain diseases). Without any protective measures, two of the five apitherapists were exposed to suspected COVID-19 cases and others were exposed to confirmed COVID-19 cases, but none of them were infected eventually. None of the 121 patients were infected by SARS-CoV-2, and three of them had close contact with immediate family members who were confirmed SARS-CoV-2 Infection cases. It might be supposed that beekeepers are less likely to be exposed to SARS-CoV-2 because they live in less densely populated rural areas. But the five apitherapists and their patients are from densely populated areas in Wuhan. These people have one thing in common: they develop a tolerance to bee sting.

Bee sting can cause allergic reactions (Park and Lee, 2016), and it can even lead to death due to the excessive stress response of the immune system (Vasquez-Revuelta et al., 2018). Bee venom can affect the body's immune system (Cherniak and Govorushko, 2018) and enhance the differentiation of human regulatory T cells (Caramalho et al., 2015), which play an important role in control of SARS-CoV infection (Chen et al., 2010). Does the stimulation of the immune system caused by bee venom reduce susceptibility to SARS-CoV-2? To test this, animal experiments would be needed. Monkeys might be suitable for this study. Monkeys could be divided into two experimental groups with the same breed and age. One group could be made tolerant-to bee venom after a period of daily bee stings, while the other

group receives no intervention. They could then be raised in the same environment contaminated by SARS-CoV-2, and multiple tests performed to see if they were infected by SARS-CoV-2.

Our purpose in writing this letter is to ask scholars with appropriate research conditions to test this assumption. In the absence of vaccine of SARS-CoV-2, if this method works, then it could offer one hope towards victory over COVID-19.

References

1. Bennett M, Baxby D. Cowpox. *J Med Microbiol.* 1996 Sep;45(3):157-8.
2. Park HS, Lee JH. Granulomatous Inflammation Induced by Bee Sting. *JAMA Ophthalmol.* 2016 Aug 11;134 (8): e161024.
3. Vazquez-Revuelta P, Madrigal-Burgaleta R. Death due to Live Bee Acupuncture Apitherapy. *J Investig Allergol Clin Immunol.* 2018; 28 (1): 45-6
4. Cherniack EP, Govorushko S. To bee or not to bee: The potential efficacy and safety of bee venom acupuncture in humans. *Toxicon.* 2018 Nov; 154: 74-8.
5. Caramalho I, Melo A, Pedro E, Barbosa MM, Victorino RM, Pereira Santos MC, Sousa AE. Bee venom enhances the differentiation of human regulatory T cells. *Allergy.* 2015 Oct; 70 (10): 1340-5.6
6. Chen J, Lau YF, Lamirande EW, Paddock CD, Bartlett JH, Zaki SR, Subbarao K. Cellular immune responses to severe acute respiratory syndrome coronavirus (SARS-CoV) infection in senescent BALB/c mice: CD4+ T cells are important in control of SARS-CoV infection. *J Virol.* 2010 Feb;84(3):1289-301.

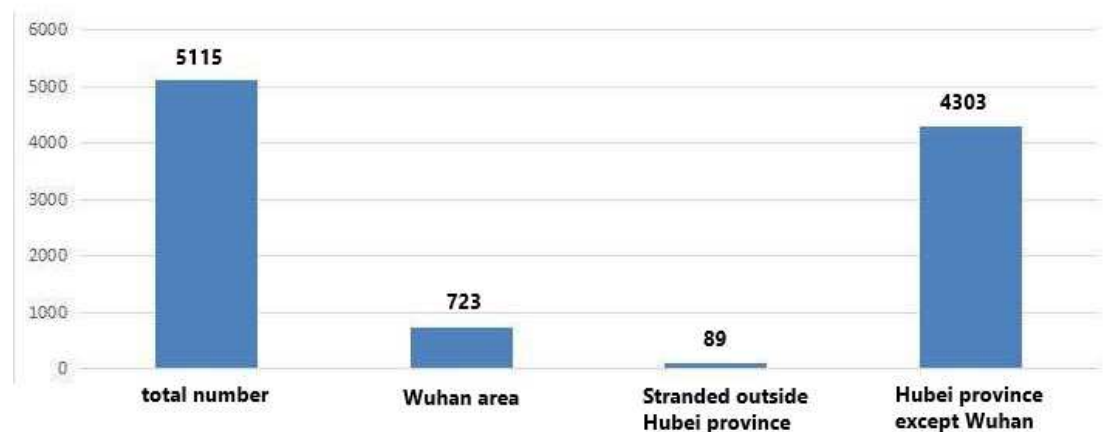


Figure 1

Conflicts of Interest: The authors have no conflicts of interest to declare. The survey data of beekeepers in Hubei province were provided by professor Fu-liang Hu, an expert of apiology. Dr. Xu gave me a lot of support on my task of the prevention and control of coronavirus.

The research conforms to moral and ethical norms.

Project number of the funding: 0020190293.